

Evidence summary and table

Project Title: Interventions to address potentially inappropriate prescriptions for older adults in primary care

Subtitle: Effectiveness of interventions to reduce potentially inappropriate prescribing (PIP) in older adults

Problem: Potentially inappropriate prescriptions (PIPs)

Intervention: Any intervention aimed at reducing PIPs, including reviews by health care providers who were either part of or independent of the clinical team.

Comparison: Usual care or minimal interventions (e.g. generic reminders about safe prescribing).

Main Outcomes: Number of medications, non-serious adverse drug reactions, injurious falls, quality of life, medical visits, emergency department visits, hospitalizations, all-cause mortality.

Background

Potentially inappropriate prescribing (PIP), defined as prescribing medications where risks outweigh benefits or without a clinical indication, is a significant issue among older adults, contributing to adverse outcomes such as hospitalization and mortality. The prevalence of PIP increases with the number of medications prescribed, making polypharmacy a key contributor. Deprescribing, a shared decision-making process involving the reduction or discontinuation of inappropriate medications, addresses known barriers faced by both prescribers and patients, such as time constraints, communication challenges, and fear of stopping medications. We conducted a systematic review to evaluate the effectiveness of interventions designed to address PIP, including implicit and explicit approaches, in reducing medication burden and improving outcomes such as hospitalizations, mortality, and quality of life. By synthesizing evidence from 118 randomized controlled trials involving over 400,000 participants, this document aims provide actionable insights to guide evidence-based practice in primary care and inform the development of a national guideline.

Problem

Is the problem a priority? (Judgement: Yes)

PIP is associated with serious harms in older adults. One systematic review found that potentially inappropriate medication (PIM) use increased mortality in older adults by 1.6-fold.¹ Additionally, a study analyzing a census of pharmaceutical claims in Germany demonstrated that PIMs are correlated with high rates of adverse drug events resulting in hospitalizations.² Furthermore, patients themselves express a preference for taking fewer medications, citing concerns such as cost, convenience, and the risk of adverse drug events.³ For instance, an internet-based cross-sectional study found that patients are willing to pay an average of \$1445 USD to avoid taking a pill daily, underscoring their desire to take fewer medications.⁴

Desirable Effect

How substantial are the desirable anticipated effects? (Judgement: Moderate)

Research Evidence

PIP Interventions

Interventions aimed at addressing PIPs often involve deprescribing, which may include stopping medicines entirely, reducing doses, or changing to alternative therapies. These interventions are designed to address the tendency of both patients and providers to continue medications where the risks may outweigh the harms. Several randomized controlled trials conducted internationally have assessed the effectiveness of PIP interventions in reducing polypharmacy in older adults by employing a variety of interventions, including medication reviews,⁵⁻⁷ medication reconciliation,⁸ education programs,⁹⁻¹¹ audit and feedback programs,¹² computerized software tools,¹³⁻¹⁴ and computerized decision support tools.¹⁵⁻¹⁷

Our systematic review provides evidence for the benefits and effectiveness of interventions to address PIP in older adult outpatients, as reported in randomized controlled trials. Our review includes studies assessing any intervention aimed at reducing PIPs, whether led by healthcare providers integrated into clinical teams or operating independently.

Outcome measures included number of medicines, non-serious adverse reactions, injurious falls, quality of life, medical visits, emergency department visits, hospitalizations, and all-cause mortality.

Summary of findings table: PIP interventions

| Outcome | Plain language statement | With PIP intervention | Usual care | Relative effect (95% CI) | Absolute effect | Certainty of evidence (GRADE) |
|-------------------------------|--|--|--|------------------------------------|------------------------|--------------------------------------|
| Number of medicines | PIP interventions were associated with a reduction in the number of medications prescribed. | Mean number of medicines: 9.4 | Mean number of medicines: 9.9 | SMD: -0.25 (95% CI -0.38 to -0.13) | -0.5 | High |
| Non-serious adverse reactions | There is no association between PIP interventions and the proportion of patients experiencing a non-serious adverse drug reaction. | Rate of non-serious adverse reactions: 50.7% | Rate of non-serious adverse reactions: 33.2% | RR: 0.92 (95% CI 0.58 to 1.46) | 17.5% | Very low |
| Injurious falls | There is no association between PIP interventions and the number of injurious falls. | Median falls per 100 patients: 3.5 | Median falls per 100 patients: 3.2 | SMD: 0.01 (95% CI -0.12 to 0.14) | 0.3 | Low |
| Quality of life | There is no association between PIP interventions and quality of life. | Not calculable | Not calculable | SMD: 0.09 (95% CI -0.04 to 0.23) | Not calculable | Low |
| Medical visits | There is no association between PIP interventions and the number of medical outpatient visits. | Rate of medical outpatient visits: 5.6% | Rate of medical outpatient visits: 5.5% | SMD: 0.02 (95% CI -0.02 to 0.07) | 0.1 | Low |
| Emergency department visits | There is no association between PIP interventions and emergency department visits. | Rate of emergency department visits: 23.2% | Rate of emergency department visits: 24.3% | RR: 1.02 (95% CI 0.96 to 1.08) | -1.1 | Low |
| Hospitalizations | There was a slight reduction in hospitalization that was not statistically significant. | Hospitalization rate: 53.1% | Hospitalization rate: 43.1% | RR: 0.95 (95% CI 0.89 to 1.02) | -10% | Low |
| All-cause mortality | There was a slight reduction in all-cause mortality that was not statistically significant. | Rate of all-cause mortality: 13.2% | Rate of all-cause mortality: 13.8% | RR: 0.94 (95% CI 0.85 to 1.04) | -0.6% | Moderate |

Narrative Summary

Outcome 1: Number of medicines

Our systematic review, which included data from 118 randomized controlled trials and comprised 417, 412 patients, showed that PIP interventions reduced the number of medicines prescribed to by approximately 0.4 medicines per patient. Of the 118 trials included, 48 trials reported the number of prescribed medicines as an outcome, and of those, 43 trials were statistically pooled (SMD -0.25; 95 % CI -0.38 to -0.13; $I^2 = 90\%$, $n=16,174$). One randomized controlled trial reported a reduction in the number of medicines at 3 months that was not sustained at 12 months, but overall, reductions were generally maintained over the full trial duration.¹⁸

Outcome 2: Non-serious adverse reactions

PIP interventions did not significantly affect the proportion of participants experiencing non-serious adverse reactions. This finding is based on data pooled from three trials (RR 0.92; 95% CI 0.58 to 1.46, $I^2 = 0\%$, $n=841$).

Outcome 3: Injurious falls

PIP interventions showed no correlation with changes in the number of injurious falls, as evidenced by meta-analysis of 21 out of 24 trials (SMD 0.01; 95 % CI -0.12 to 0.14; $I^2=80\%$, $n=10,963$). A vote count of the 3 trials that could not be statistically pooled revealed that two reported fewer falls in the intervention group.

Outcome 4: Quality of life

There was no significant associations between PIP interventions and patient quality of life when pooling data from 35 out of 37 trials (SMD 0.09; 95% CI, -0.04 to 0.23, $I^2=80\%$, $n=12,221$). Quality of life measures included tools such as the EuroQol 5 Dimension ($n=27$, 73%), the 36-Item Short Form Survey ($n=4$, 11%), the 12-Item Short Form Survey ($n=3$, 8%), and the QUALID scale ($n=1$, 3%). Of two unpooled trials, both reported reduced quality of life scores in the intervention group.

Outcome 5: Medical visits

No significant association was found between PIP interventions and outpatient medical visits, based on pooled data from 10 of 18 trials (SMD 0.02; 95% CI -0.02 to 0.07; $I^2 = 0\%$, $n = 5,341$). Of the unpooled trials, two reported fewer outpatient visits in the intervention group, five showed more, and one found no difference.

Outcome 6: Emergency department visits

There was no association between PIP interventions and emergency department visits in a meta-analysis of 11 trials (RR 1.02; 95% CI 0.96 to 1.08; $I^2 = 0\%$, $n = 5,853$). Of five unpooled trials, two reported fewer emergency visits, while three reported more.

Outcome 7: Hospitalizations

A small, non-significant reduction in hospitalizations was observed in a meta-analysis of 22 out of 43 trials (RR 0.95; 95% CI 0.89 to 1.02; $I^2 = 45\%$, $n = 57,636$). Of 21 unpooled trials, 11 reported fewer admissions, six reported more, and four found no effect.

Outcome 8: All-cause mortality

A slight, non-significant reduction in all-cause mortality was found when pooling data from 47 trials (RR 0.94; 95% CI 0.85 to 1.04; $I^2 = 0\%$, $n = 16,682$). In the 6 articles not pooled, 2 reported fewer deaths in the intervention group, 1 reported fewer deaths in the control group, and 3 reported no effect.

Recommendations that could be adapted to this guideline:

Undesirable effects

How substantial are the undesirable anticipated effects? (*Judgement: Small for all interventions*)

Certainty of evidence

What is the overall certainty of the evidence of effects? (*Judgement: Low to Moderate*)

The certainty of evidence is high for the reduction in the number of medications prescribed but low for outcomes like quality of life, adverse drug reactions, and injurious falls.

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison? (*Judgement: Favours the intervention*)

The reduction in the number of medications prescribed without substantial harm suggests that the desirable effects outweigh any potential risks.

Values

Is there important uncertainty about, or variability in, how much people value the main outcomes? (*Judgement: Low uncertainty*)

Evidence suggests that patients value reducing medication burden.

Resources required

What is the certainty of the evidence of resource requirements (costs)? (*Judgement: Low to Moderate*)

Interventions like deprescribing may require additional time and effort from healthcare providers, which could vary across settings.

Cost-effectiveness

Does the cost-effectiveness of the option favour the option or the comparison? (*Judgement: Favours the option*)

Systematic reviews indicate that most deprescribing interventions are cost-saving or cost-effective, particularly those led by pharmacists and physicians.

Equity

What would be the impact on health equity? (*Judgement: Probably increases equity*)

PIP interventions could improve access to safer prescribing practices for older adults, especially in underserved populations, by reducing medication-related harms and costs.

Acceptability

Are PIP interventions acceptable to key stakeholders? (Judgement: Likely acceptable)

Based on a systematic review of controlled trials we conducted assessing the acceptability of PIP interventions, PIP interventions are at least acceptable to patients, based on reports of patient satisfaction and documented discussions with patients about deprescribing. In our review, patient satisfaction was reported in 7 studies, in which 5 of them reported higher satisfaction in the intervention arm. There was no statistically significant difference in patient satisfaction between groups, with the point estimate consistent with slightly higher satisfaction with PIP interventions (SMD 0.45; 95 % CI -0.14 to 1.04, $I^2=96\%$, $n = 4,414$). Our systematic review also included 2 studies that, although did not directly report patient satisfaction as an outcome, provided the proportion of patients who discussed medicine discontinuation with a provider. Both studies reported that such discussions are more likely to be initiated by patients who receive PIP interventions.¹⁹⁻²⁰

Feasibility

Are PIP interventions feasible to implement? (Judgement: Likely feasible)

Evidence suggests that many PIP interventions, such as pharmacist- or physician-led reviews, can be effectively integrated into primary care and nursing home settings. Trials like D-PRESCRIBE and the OPTI-SCRIPT study have demonstrated successful implementation with measurable outcomes, and systematic reviews highlight the adaptability of these approaches across different healthcare contexts.²¹⁻²²

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